

# Acute Seizure in a Dog

**Erin Y. Akin, DVM, DACVIM (Neurology)**

*Bush Veterinary Neurology Service*

*Woodstock, Georgia*



## THE CASE

A 7-year-old spayed golden retriever is presented after a seizure lasting 30 to 60 seconds. During the seizure, the dog fell onto her left side and paddled her legs; her head and neck were extended, she appeared to be unconscious and unresponsive, and she urinated. Salivation was profuse. After the seizure, the dog vomited, appeared blind and disoriented, and paced around the house. One hour later, she returned to normal and had a ravenous appetite.

The patient has no history of seizures, but on further questioning, the owner reports the dog recently has been less active and appears to “stare off into space.” To the owner’s knowledge, the dog has not gotten into any toxins, and there is no history of diarrhea, coughing, or sneezing. Appetite is inconsistent but good—normal for this patient. There is no out-of-state travel history, and the dog is up-to-date on vaccinations and parasite preventives. There is no major medical history other than a right cranial cruciate ligament rupture that was surgically repaired via tibial plateau-leveling osteotomy 3 years prior.

Physical examination findings are unremarkable, and vital parameters are within reference range. A detailed neurologic examination is unremarkable and reveals no neurologic deficits. The dog is visual. The owner agrees to CBC, serum chemistry profile, urinalysis, and a thyroid panel; all are unremarkable and fall within reference range. Considerations include structural brain disease and idiopathic epilepsy. Metabolic and systemic diseases that can cause seizures are considered less likely based on diagnostic testing results.

## THE CHOICE IS YOURS ...

### CASE ROUTE 1

To monitor the dog for the rest of the day, begin treatment with oral anticonvulsant medication, and send her home for further monitoring, see page 26.

### CASE ROUTE 2

To perform a preanesthetic workup and brain MRI, +/- CSF tap and analysis, +/- infectious disease testing, see page 28.

## CASE ROUTE 1

The owner agrees to keep the dog at the hospital for the rest of the day, begin treatment with oral anticonvulsant medication, and take her home for further monitoring.

### Case Progression

You place a cephalic vein catheter, hospitalize the dog for the day, and place the dog on seizure watch. The first dose of phenobarbital is administered (2.5 mg/kg IV). On discharge that evening, there have been no more seizures, and the dog's neurologic examination is normal. You prescribe phenobarbital (2.5 mg/kg PO q12h) and instruct the owner to keep a seizure log to record pertinent details (eg, time of day, length of seizure, description of seizure, association with food or stress, medication side effects). Commonly seen side effects of phenobarbital (eg, lethargy, ataxia, increased drinking, increased urinating, increased appetite) and longer-term side effects (eg, hepatopathy, bone marrow suppression [rare]) are discussed with the owner. You ask the owner to record a video of an episode, if possible, and recommend a recheck in 2 to 3 weeks to perform CBC, serum chemistry profile, and phenobarbital-level tests.<sup>1</sup>

### Clinical Considerations

Several factors must be considered for a patient presenting with seizures, including the potential cause of the seizures, diagnostic testing options, owner intent and financial considerations, the patient's overall general health, and any concurrent diseases. The dog in this case is being treated empirically for seizures without further diagnostic investigation. In humans, evidence suggests no benefit to starting anticonvulsant therapy after a single event without known cause.<sup>2</sup> However, evidence also suggests that long-term outcome may be improved when anticonvulsant medications are started earlier.<sup>3</sup>

Practitioners often associate patient age at seizure onset with underlying cause. Idiopathic epilepsy is commonly suspected when patient age at seizure onset is between 6 months and 5 years.<sup>4</sup> When evaluating first-time seizures in older dogs, an underlying pathologic process in the brain (eg, neoplasia) is often high on the list of differential diagnoses.<sup>5</sup> However, in a recent study, although a majority of older dogs were diagnosed with clinical epilepsy, 23% to 45% of older dogs with late-onset seizures were diagnosed with primary epilepsy and, perhaps, could have a better prognosis than anticipated.<sup>6</sup>

### Outcome

The dog is discharged and returns for a recheck 3 weeks later. There have been no seizures, and all blood work is within commonly accepted laboratory reference ranges. At the 3-month recheck, no additional seizures are reported. However, shortly thereafter, the dog goes into status epilepticus and is taken to a local emergency clinic. Despite aggressive emergency treatment, the dog dies. The owner consents to a postmortem examination at a local veterinary school. On necropsy, a large mass in the left frontal lobe is found and is histologically confirmed to be a meningioma.

### Your Choice's Implications

Treating seizures empirically with oral medication is common and appropriate in veterinary medicine—particularly when there are financial constraints—in first-time seizure patients, and when idiopathic epilepsy is high on the list of differential diagnoses. This was not an inappropriate approach. Most anticonvulsant medications are readily available, are easy for owners to administer at home in tablet or liquid form, and show some degree of efficacy. Both phenobarbital and potassium bromide are reasonable first-line anticonvulsants in dogs<sup>7</sup> in addition to levetiracetam and zonisamide.<sup>8</sup>

## CASE ROUTE 2

The owner elects to perform a preanesthetic workup and brain MRI, +/- CSF tap and analysis, +/- infectious disease testing.

### Case Progression

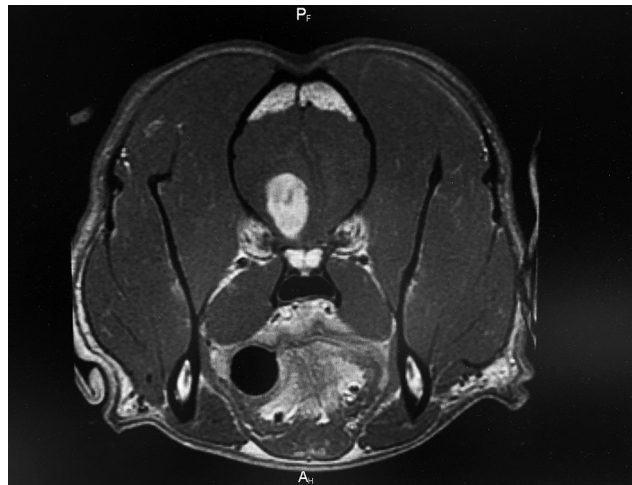
The owner consents to a preanesthetic diagnostic investigation, including 3-view thoracic radiography and abdominal ultrasonography followed by referral to a local specialty center for a brain MRI. The radiographs and ultrasound are unremarkable and show no evidence of primary or metastatic neoplasia. Brain MRI reveals a T2 hyperintense, T1 hypointense, vividly contrast-enhancing mass in the left frontal lobe consistent with a meningioma (*Figure*).<sup>9</sup> Mild peritumoral edema is noted. CSF tap and infectious disease testing are not performed.

Mannitol is administered (1 g/kg IV over 15 minutes), and the dog recovers uneventfully from anesthesia. She is given an injection of phenobarbital (2.5 mg/kg IV), prescribed phenobarbital (2.5 mg/kg PO q12h), and started on an anti-inflammatory dose of prednisone. A recheck is recommended in 2 to 3 weeks for CBC, serum chemistry profile, and phenobarbital-level tests.<sup>1</sup>

Treatment options for presumed meningioma are discussed with the owner and include palliative therapy, surgical debulking of the mass with samples submitted for histopathology, radiation therapy, chemotherapy, and combinations of these therapies. The owner elects surgical debulking of the mass followed by radiation therapy. Histopathology of the debulked material indicates a meningioma.

### Clinical Considerations

Because complete neurologic assessments with advanced imaging can be cost-prohibitive, many owners may forgo further testing and elect empirical treatment.<sup>6</sup> The owner in this case was able to move forward and therefore had additional information that could



▲ **FIGURE** T1 MRI image showing contrast-enhancing left forebrain meningioma. Photo courtesy of Casey Neary, DVM, DACVIM (Neurology), Bush Veterinary Neurology Service

help in making decisions about the dog's treatment. Advanced imaging is recommended in most seizure cases, regardless of the dog's age, to rule out structural causes of intracranial disease.

Meningiomas are the most common intracranial tumor in dogs; dolichocephalic breeds may be at increased risk.<sup>10</sup> Meningiomas are typically considered to be a neoplasm of older dogs, but they have been diagnosed in dogs as young as 16 months of age.<sup>9</sup> Clinical signs in dogs are location-dependent; among the most common are seizures.

Surgery, radiation, and chemotherapy target the primary tumor, whereas palliative therapy targets the secondary effects of the tumor and generally consists of administering anticonvulsants and glucocorticoids.<sup>9,11</sup> Radiation therapy in combination with surgical debulking of intracranial meningiomas has been shown to extend the median survival time in dogs.<sup>10</sup> There is

# GALLIPRANT® (grapiprant tablets)

## For oral use in dogs only

### 20 mg, 60 mg and 100 mg flavored tablets

#### A prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) EP<sub>4</sub> receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

**Caution:** Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**Before using this product, please consult the product insert, a summary of which follows:**

**Indication:** GALLIPRANT (grapiprant tablets) is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

**Dosage and Administration:** Always provide "Information for Dog Owners" Sheet with prescription. Use the lowest effective dose for the shortest duration consistent with individual response.

The dose of GALLIPRANT (grapiprant tablets) is 0.9 mg/lb (2 mg/kg) once daily.

GALLIPRANT tablets are scored and dosage should be calculated in half tablet increments. Dogs less than 8 lbs (3.6 kgs) cannot be accurately dosed. See product insert for complete dosing and administration information.

**Contraindications:** GALLIPRANT should not be used in dogs that have a hypersensitivity to grapiprant.

**Warnings:** Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans. **For use in dogs only.** Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

**Precautions:** The safe use of GALLIPRANT has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, or in pregnant or lactating dogs. Adverse reactions in dogs receiving GALLIPRANT may include vomiting, diarrhea, decreased appetite, mucoid, watery or bloody stools, and decreases in serum albumin and total protein.

If GALLIPRANT is used long term, appropriate monitoring is recommended.

Concurrent use with other anti-inflammatory drugs has not been studied. Concomitant use of GALLIPRANT with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after a daily dose of GALLIPRANT, a non-NSAID/non-corticosteroid class of analgesic may be necessary.

The concomitant use of protein-bound drugs with GALLIPRANT has not been studied. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications.

Drug compatibility should be monitored in patients requiring adjunctive therapy. Consider appropriate washout times when switching from one anti-inflammatory to another or when switching from corticosteroids or COX-inhibiting NSAIDs to GALLIPRANT use.

The use of GALLIPRANT in dogs with cardiac disease has not been studied.

It is not known whether dogs with a history of hypersensitivity to sulfonamide drugs will exhibit hypersensitivity to GALLIPRANT. GALLIPRANT is a methylbenzenesulfonamide.

**Adverse Reactions:** In a controlled field study, 285 dogs were evaluated for safety when given either GALLIPRANT or a vehicle control (tablet minus grapiprant) at a dose of 2 mg/kg (0.9 mg/lb) once daily for 28 days. GALLIPRANT-treated dogs ranged in age from 2 yrs to 16.75 years. The following adverse reactions were observed:

Adverse reaction*	GALLIPRANT (grapiprant tablets) N = 141	Vehicle control (tablets minus grapiprant) N = 144
Vomiting	24	9
Diarrhea, soft stool	17	13
Anorexia, inappetence	9	7
Lethargy	6	2
Buccal ulcer	1	0
Immune mediated hemolytic anemia	1	0

\*Dogs may have experienced more than one type or occurrence during the study.

GALLIPRANT was used safely during the field studies with other concurrent therapies, including antibiotics, parasiticides and vaccinations.

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>

**Information for Dog Owners:** Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, and decreasing albumin and total protein. Appetite and stools should be monitored and owners should be advised to consult with their veterinarian if appetite decreases or stools become abnormal.

**Effectiveness:** Two hundred and eighty five (285) client-owned dogs were enrolled in the study and evaluated for field safety. GALLIPRANT-treated dogs ranging in age from 2 to 16.75 years and weighing between 4.1 and 59.6 kgs (9-131 lbs) with radiographic and clinical signs of osteoarthritis were enrolled in a placebo-controlled, masked field study. Dogs had a 7-day washout from NSAID or other current OA therapy. Two hundred and sixty two (262) of the 285 dogs were included in the effectiveness evaluation. Dogs were assessed for improvements in pain and function by the owners using the Canine Brief Pain Inventory (CBPI) scoring system. A statistically significant difference in the proportion of treatment successes in the GALLIPRANT group (63/131 or 48.1%) was observed compared to the vehicle control group (41/131 or 31.3%). GALLIPRANT demonstrated statistically significant differences in owner assessed pain and function. The results of the field study demonstrate that GALLIPRANT, administered at 2 mg/kg (0.9 mg/pound) once daily for 28 days was effective for the control of pain and inflammation associated with osteoarthritis.

**Storage Conditions:** Store at or below 86° F (30° C)

**How Supplied:** 20 mg, 60 mg, 100 mg flavored tablets in 7, 30 and 90 count bottles.

NADA 141-455, Approved by FDA

US Patents: 6,710,054; 7,960,407; 9,265,756

Made in New Zealand. Manufactured for: Aratana Therapeutics, Inc., Leawood, KS 66211

Reference: 1. [http://www.vet.upenn.edu/docs/default-source/VVIC/canine-bpi\\_userguide.pdf?sfvrsn=0](http://www.vet.upenn.edu/docs/default-source/VVIC/canine-bpi_userguide.pdf?sfvrsn=0)

Additional information is available at 1-888-545-5973.

GALLIPRANT is a trademark of Aratana Therapeutics, Inc.

© Aratana Therapeutics, Inc. June 2016



Brief Summary: AT1-040-16

limited information about survival time with the use of chemotherapy on intracranial neoplasms in dogs; lomustine and hydroxyurea are sometimes used.<sup>9,12</sup>

## Outcome

The dog recovers from surgery uneventfully and is treated with a commonly accepted radiation protocol. She continues on phenobarbital and survives another 18 months with good quality of life.

## Your Choice's Implications

Advanced diagnostics provided useful information in this case with a presumptive diagnosis of meningioma. Biopsy was needed for definitive diagnosis,<sup>9</sup> and meningioma was confirmed. Long-term anticonvulsant therapy and glucocorticoids are still indicated. Because of pursuing advanced diagnostics, which were followed by aggressive surgical and radiation treatment, this dog lived another 18 months. ■■■

## References

- Podell M, Volk HA, Berendt M. 2015 ACVIM small animal consensus statement on seizure management in dogs. *J Vet Intern Med.* 2016;30(2):477-490.
- Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: management of an unprovoked first seizure in adults. *Neurology.* 2015;84(16):1705-1713.
- Brodie MJ, Barry SJ, Bamagous GA, Norrie JD, Kwan P. Patterns of treatment response in newly diagnosed epilepsy. *Neurology.* 2012;78(20):1548-1554.
- Thomas WB. Idiopathic epilepsy in dogs and cats. *Vet Clin North Am Small Anim Pract.* 2010;40(1):161-179.
- Schwartz M, Muñana KR, Nettifee-Osborne J. Assessment of the prevalence and clinical features of cryptogenic epilepsy in dogs: 45 cases (2003-2011). *J Am Vet Med Assoc.* 2013;242(5):651-657.
- Ghormley TM, Feldman DG, Cook JR Jr. Epilepsy in dogs five years of age and older: 99 cases (2006-2011). *J Am Vet Med Assoc.* 2015;246(4):447-450.
- Boothe DM, Dewey C, Carpenter DM. Comparison of phenobarbital with bromide as a first-choice antiepileptic drug for treatment of epilepsy in dogs. *J Am Vet Med Assoc.* 2012;240(9):1073-1083.
- Dewey CW. Anticonvulsant therapy in dogs and cats. *Vet Clin North Am Small Anim Pract.* 2006;36(5):1107-1127, vii.
- Adamo F, Forrest LJ, Dubielzig R. Canine and feline meningiomas: diagnosis, treatment and prognosis. *Compend Contin Educ Pract Vet.* 2004;26(12):951-965.
- Axlund TW, McGlasson ML, Smith AN. Surgery alone or in combination with radiation therapy for treatment of intracranial meningiomas in dogs: 31 cases (1989-2002). *J Am Vet Med Assoc.* 2002;221(11):1597-1600.
- Sessums K, Mariani C. Intracranial meningioma in dogs and cats: a comparative review. *Compend Contin Educ Vet.* 2009;31(7):330-339.
- Hu H, Barker A, Harcourt-Brown T, Jeffery N. Systematic review of brain tumor treatment in dogs. *J Vet Intern Med.* 2015;29(6):1456-1463.